Active Sensing & Active Coping using Stochastic Resonance

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Decision making is a routine cognitive function whose underlying neurobiological mechanisms are presently unclear. In humans, damage to parts of the prefrontal cortex was associated with prolonged deliberation over choices, as well as with impulsive, risky behaviour. Here we suggest a simplified neural circuit, that chooses a given motor action by weighing the efforts and rewards expected from it. The circuit, involving prefrontal & amygdalar components, is fed by a regulated noisy input, that enables reaching decisions at times of uncertainty via stochastic resonance.

1. Introduction

It is presently unclear how expected costs and rewards are weighted during response selection [30,36]. In humans, damage to parts of the prefrontal cortex was associated with prolonged deliberation over choices, as well as with impulsive, risky behaviour [30-32]. Both the anterior cingulate cortex (ACC) and the orbitofrontal cortex (OFC) have been shown to be involved in declarative decision-making regarding motor actions [27-36,41-2]. In this work we shall analyze the following motor-sensory-motor loop, which involves both amygdalar and prefrontal components:

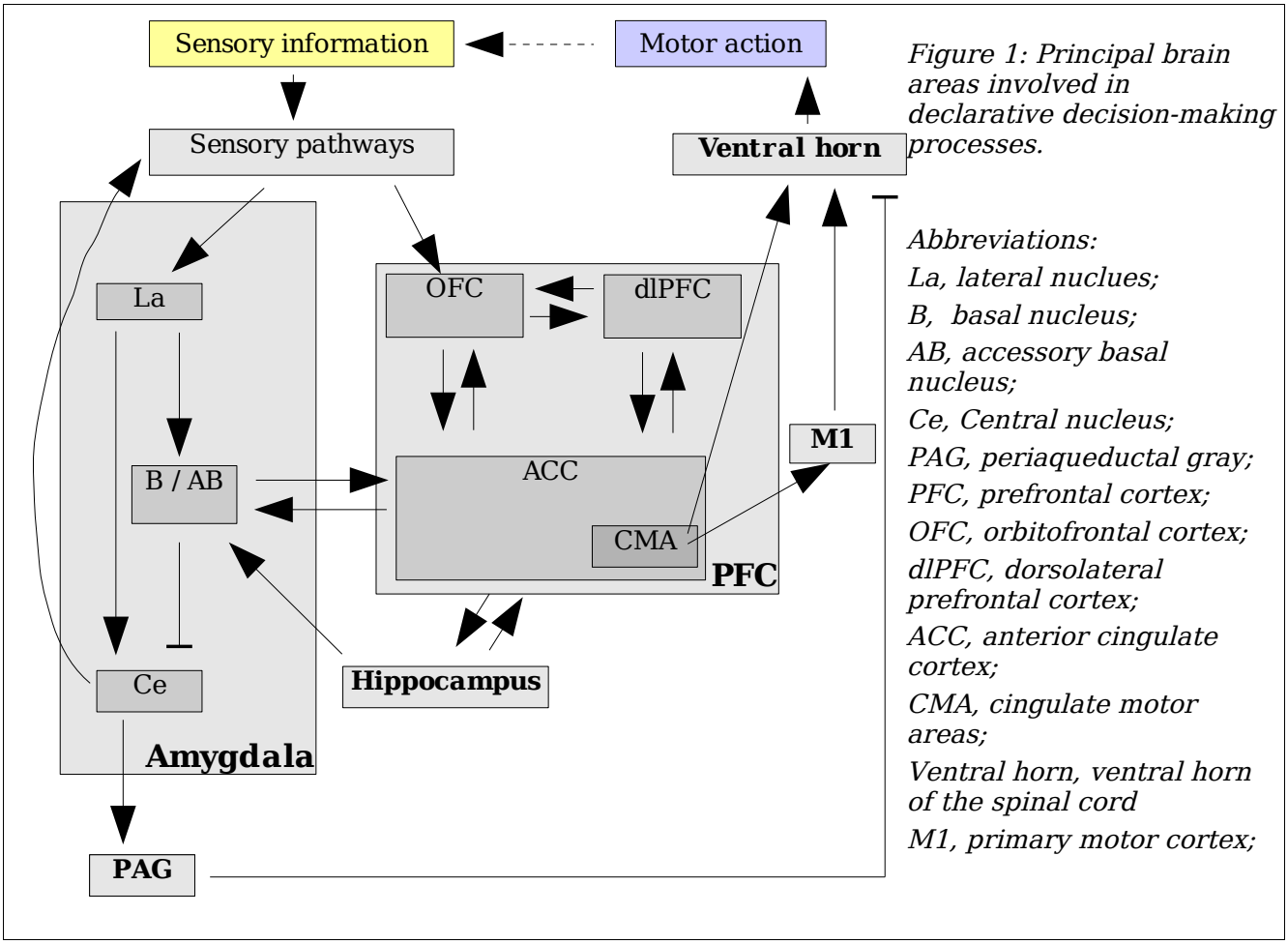

Figure 1: Principal brain areas involved in declarative decision-making processes.

Abbreviations:
La, lateral nuclues;
B, basal nucleus;
AB, accessory basal nucleus;
Ce, Central nucleus;
PAG, periaqueductal gray;
PFC, prefrontal cortex;
OFC, orbitofrontal cortex;
dlPFC, dorsolateral prefrontal cortex;
ACC, anterior cingulate cortex;
CMA, cingulate motor areas;
Ventral horn, ventral horn of the spinal cord
M1, primary motor cortex;

The loop enables the comparison of two competing signals. One signal urges to execute a suggested motor action to gain a reward, whereas the other urges to avoid it to spare the effort it takes. For high rewards and low efforts, the proposed motor action is executed and the amygdalar fearful reaction is inhibited. For low rewards and high efforts, the proposed motor action is not executed, and the amygdalar response is reinforced. The loop should reach a decision within a limited amount of time, even when the expected reward and effort are both high or low.

As illustrated in figure 1, voluntary movements are initiated by cingulate motor areas (CMA) in the ACC, which project both to the primary motor cortex and to the ventral horn of the spinal cord [27,29]. These motor pathways are suggestively used by the ACC to elicit exploratory actions, in order to acquire more information about the environment and the potential reward [29]. The resulting sensory information is fed both to the lateral nucleus of the amygdala (La), and to the OFC. The OFC projects directly to the ACC, whereas the lateral nucleus projects to the basal (B) and accessory basal (AB) nuclei, which project to the ACC. The B and AB nuclei play a role in evaluating the expected efforts and rewards associated with the suggested action. Hippocampal innervations to the B and AB nuclei enable the organism to contextualize its reaction to the sensory input [19].

The central nucleus of the amygdala (Ce) projects back to the earliest stages of the various sensory processing pathways that innervate the La nucleus [19]. Hence, the amygdala regulates the cortical areas that project to it, directly controlling its cortical input. It also affects its sensory input indirectly by triggering an alarming orienting response, which enables one to process a salient stimulus even when attention is fixed elsewhere [18-19]. The Ce is capable of triggering a freezing response to a fearful stimulus via its innervations to the midbrain's periaqueductal gray (PAG). The ACC can inhibit this response via its innervations to the B & AB nuclei [25-26]. As the B & AB nuclei are functionally indistinguishable for the purpose of this work, we shall hereafter treat them as a single component B.

2. Implementation

Having denoted the connectivity of the various areas involved in decision making, we suggest a corresponding circuit which may enable to make motor action decisions in effort-based tasks. The circuit compares two competing signals – an effort e(t) and a reward r(t) (figure 2). Both are formalized in the amygdala based on incoming sensory input, then normalized in the ACC with respect to reference values e_{ref} & r_{ref}. The resulting normalized signals S(t) and R(t) are fed into an (SR)' flip flop switch with additive noisy inputs N(t). The flip flop switch, implemented by two mutually inhibitory populations of neurons [22-24], regulates the execution of the suggested motor action. Its output Q is sent both to cingulate motor areas (CMA) in the ACC and to the basal nucleus of the amygdala, which inhibits the freezing response initiated by the central nucleus.

While the inputs S(t) and R(t) to the flip flop are suggested to arrive from the ACC, there are several reasons to suggest that the flip flop is still operational in the absence of a functional ACC. First, ACC lesions in rats did not affect their performance in delay-based decision making tasks, believed to involve the OFC [35,29]. Moreover, in effort-based tasks, the same ACC lesions biased the rats to choose smaller rewards requiring lesser effort. This finding conforms with an intact flip flop circuit that receives an insufficient reward (R) input, rather than a non-operational flip flop. The ACC may compute the contextual value of each option, as suggested earlier [28], but it does not seem to choose among the weighted options. Given that prefrontal lesions have been associated

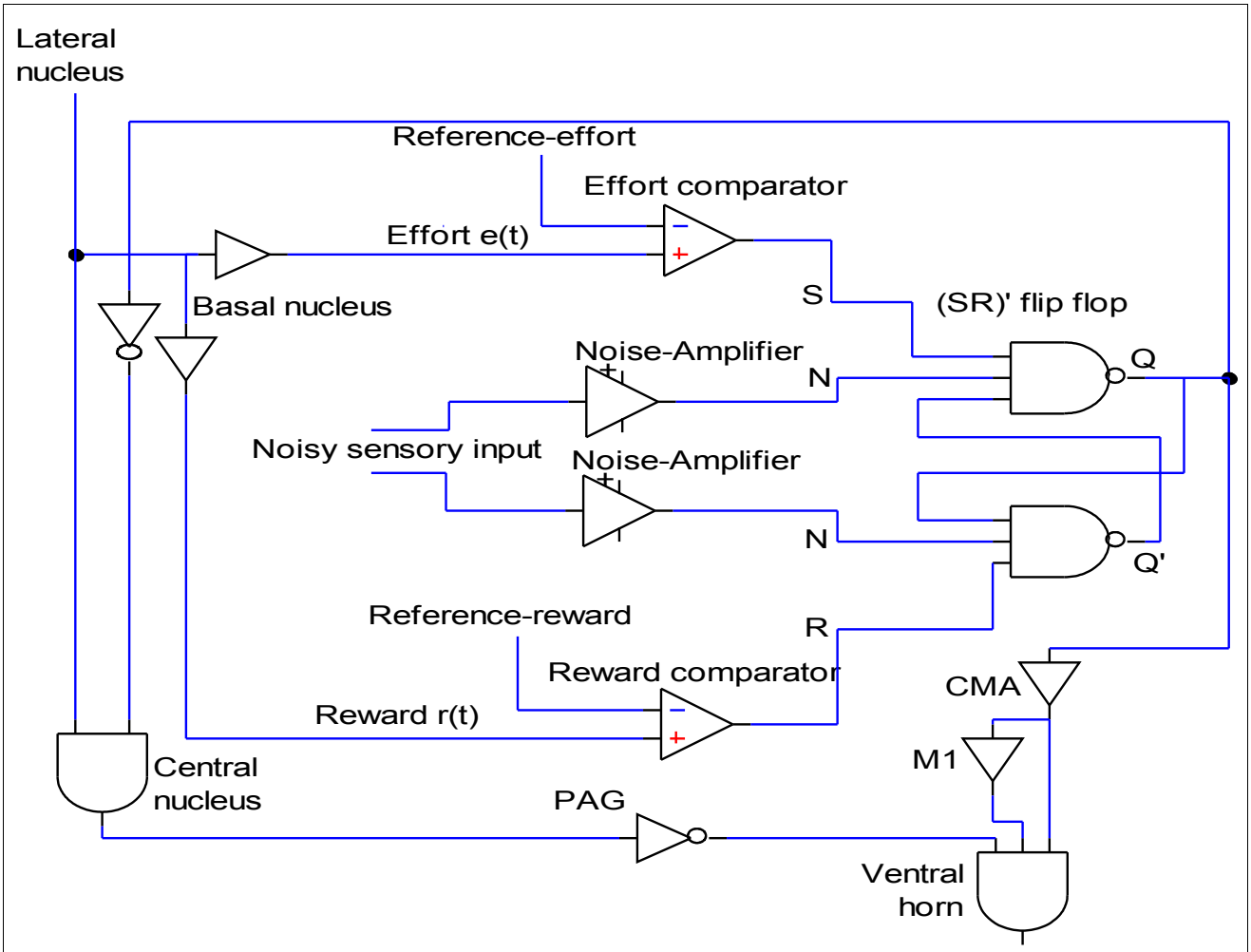

Figure 2: Simplified decision making circuit for effort-based tasks. The amygdalar nuclei are denoted on the left. A noisy (SR)' flip flop is implemented in the ventromedial PFC. Its output is sent both to the CMA and back in to the basal nucleus of the amygdala.

with irresponsible, risky behaviour in humans [30-32], we are inclined to suggest that other prefrontal structures accommodate the inhibitory neuronal populations which constitute the hypothetical flip flop. This anatomical question thus remains open at present.

Figure 3 demonstrates the output of the flip flop switch for varying levels of effort and reward. When both inputs to an (SR)' flip flop are high, the switch retains its earlier output, a situation known as a 'keep state'. When both inputs are low, the circuit might bifurcate between high and low outputs or stay in either state for undetermined duration. The noisy input N(t) to the switch is used to rescue it of this metastability. Adding weak noisy inputs to a neuronal flip flop increases the probability that an incoming subthreshold signal will be summed with an instantaneous excitatory noisy input, thereby initiating an action potential. As in the single neuron case [8], increasing noise levels necessarily induce a higher rate of stochastic firing, irrespective of the incoming signal. Thus a zero-mean noisy input to an (SR)' flip flop could rescue it of metastability, and increase its detection probability of subthreshold signals, at the price of occasional stochastic state transitions. The optimal noise level is in itself dependent on the strength of the signal – the weaker the signal, the stronger is the r.m.s. noise level required to amplify it [9]. Therefore the r.m.s. level of noise should in itself be controlled to insure the optimal performance of a noisy flip flop circuit. A circuit regulating the noise level is exemplified in figure 4.

When the flip flop inputs S and R are both subthreshold, an optimal level of noise should suffice to bring the stronger input above threshold, while the weaker signal should remain subthreshold. For a common threshold value of T, the optimal noise level should therefore be proportional to T-(S+R)/2. As illustrated in figure 4, such proportional control may be implemented by inhibitory innervations from both S and R to the noise amplification stages.

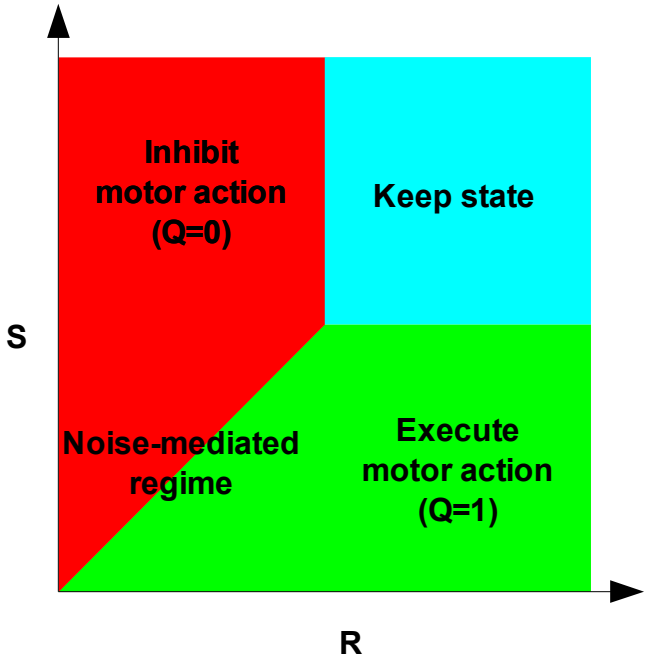

Figure 3: Flip flop output Q for varying normalized rewards (R) and efforts (S).

In addition, the noisy input is required to insure that metastability is terminated within a limited time. A monotonously rising noise level may achieve that. Thus noise level should increase with time, on top of its proportional control. This demand is analyzed in the following section.

The ACC is capable of initiating the exploratory motor actions (e.g. whisking) that shall provide additional sensory input [27], noise inclusive. The noisy sensory input may arrive via the amygdala [18-19,25], as well as via the OFC [27,29]. OFC lesions in humans were associated with prolonged deliberation in decision-making tasks, but not with degraded quality of decision making or irresponsible behaviour [32]. In the context of our model, this finding is precisely what one would expect if the noisy sensory input is mediated by the OFC. Thus we conjecture that the sensory-motor loop controlling the sensory noise level involves exploratory motor actions initiated by the ACC, causing an increased stream of sensory information to the OFC, where it may be further modulated.

While the proposed circuit may seem conspicuously complex for the specific purpose it serves, we shall argue that it is merely a limited projection of a more elaborate regulatory network. Its elements serve variable roles in different contexts, and are not specifically designed to solve effort-based decision making tasks. For instance, the ACC may implement the effort comparator in effort-based tasks, whereas the OFC may implement all or some of it in delay-based tasks. When the reward is in the form of a food pellet, the reward comparator may rely on regulatory information from the ventromedial nucleus of the hypothalamus, whereas other reward modalities shall involve other centers. Thus, as previously stressed by Rushworth et al. [27-28,35], no single organ is solely responsible for decision making. It takes an entire distributed network to enable decision making, with each type of experiment revealing but a certain facet of this network. Moreover, the proposed circuit is not suggested to be unique in its decision making capabilities, as comparable inputs to similar flip flop switches may very well exist in other neural circuits.

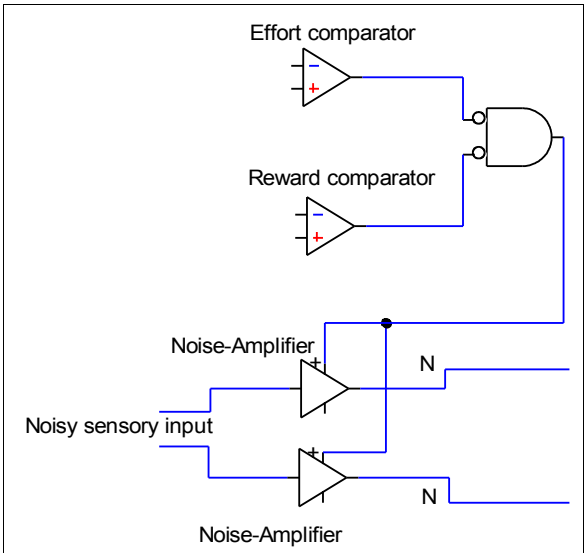

Figure 4: Noise level is in itself controlled to insure optimal signal detectability.

3. Analysis

Let **X**(t) be a vector of sensory inputs fed to the lateral nucleus of the amygdala. The lateral nucleus then produces corresponding variables e(**X**), r(**X**) representing the effort and reward it expects for the proposed motor action. These variables are fed via the basal nucleus to the ACC, where they are normalized with respect to reference values e_{ref} & r_{ref}. Let us suggest a simple proportional control for the resulting normalized signals S(t) and R(t), as follows:

(1) $$S(t)=K_{e-ACC}(K_{e-B}e(\vec{X})-e_{ref})$$

(2) $$R(t)=K_{r-ACC}(K_{r-B}r(\vec{X})-r_{ref})$$

Here, $K_{e\text{-}B}$ and $K_{r\text{-}B}$ are the gain coefficients of the basal nucleus for efforts and rewards, respectively. Similarly, $K_{e\text{-}ACC}$ and $K_{r\text{-}ACC}$ are the respective gain coefficients of the ACC for efforts and rewards. At present we ignore any long-term modification of these gain coefficients, in which the hippocampus is likely to play an additional role.

The noisy input to the flip flop is regulated in light of two functional demands – discerning small differences between efforts and rewards, and constraining the time for decision making. To satisfy the first demand, for comparable inputs S(t) and R(t), the noise level should be amplified in proportion to $(T-\frac{S}{2}-\frac{R}{2})$, where T is the common threshold value. To satisfy the other demand, the noise level should increase with time. Adding the two components yields the following proportional control for the noisy input N(t) of the flip flop:

(3) $$N(t)=n(t)\cdot\{K_{np}(T-\frac{S}{2}-\frac{R}{2})+\int_0^t K_{na}(\tau)\,d\tau\}$$

Here, n(t) is a noise source with a mean of zero, r.m.s. of v_n and a power spectral density proportional to f^{-1}. K_{np} stands for the proportional gain coefficient and $K_{na}(t)$ is a positive coefficient responsible for the incremental growth of the noise r.m.s. level. The inhibitory innervations from both S and R allow a suppression of the noise amplification stage for suprathreshold magnitudes of S and R. Equation (3) should thus be corrected to:

(4) $$N(t)=n(t)\cdot\{K_{np}\cdot max[0,(T-\frac{S}{2}-\frac{R}{2})]+\int_0^t K_{na}(\tau)\,d\tau\},\ K_{na}(t)\geq 0$$

We should stress that for input signals S and R of comparable magnitude, their sum can be more easily computed than their difference. Thus N(t) could be reliably controlled even when the difference between S and R is too small to be directly measurable.

Plugging equations (1-2) into eq. (4) yields the following explicit expression for the controlled noisy input:

(5)

$$N(t)=n(t)\cdot\{max(0,\frac{K_{np}}{2}[2\mathrm{T}-K_{e-ACC}(K_{e-B}e(\vec{X})-e_{ref})-K_{r-ACC}(K_{r-B}r(\vec{X})-r_{ref})])+\int_0^t K_{na}(\tau)d\tau\}$$

Let's inspect the loop behavior in two particular cases - $K_{np}=0$ and $K_{na}(t)\equiv 0$. In the case of $K_{np}=0$, noise level is not controlled by the magnitude of the input signals S and R. It is simply increased monotonously, eventually leading to the making of a decision. For weak S and R, such open-loop control will reach decisions more slowly than a closed-loop control ($K_{np}>0$) with the same profile of $K_{na}(t)$. Enlarging $K_{na}(t)$ to shorten the deliberation time may lead to a higher rate of incorrect decisions - action potentials first triggered in the presence of noise by the weaker signal of the two. Specifically, if $K_{np}=0, K_{na}(t)=C\,\delta(t)$, i.e. a constant noise level irrespective of stimuli and deliberation time, our model converges into earlier models of decision-making [1-5]. Wang's model [4-5] predicts that the mean decision time varies linearly with the logarithm of the signal strength. Our closed-loop control is supposed to enable faster decision making, which suits the shorter reaction times found in behavioral studies than in their simulations [5].

In the case of $K_{na}(t)\equiv 0$, noise level is tuned by K_{np} to insure optimal signal detectability. Typical deliberation times, however, may be longer than acceptable for a behaving animal. By tuning the profile of $K_{na}(t)$, the typical deliberation time may be shortened, trading fidelity for speed.

Due to the integral formulation of the dependence on $K_{na}(t)$, the integral has to be reset once a decision is reached. This reseting may be a byproduct of the motor action carried out once a decision is reached. As the temporal profile of $K_{na}(t)$ is independent of the input signals S and R, it should be experimentally reproducible along consecutive trials, thereby probing for this supposed reset mechanism. It should be noted that neurons with a monotonously rising firing rate have been experimentally recorded in the PFC [37], and specifically in CMAs of the ACC [41], an activity that has been recently modeled [21,42]. This graded activity, which lasts for seconds before resetting to baseline firing rate, may serve a role in other cognitive processes [42].

Signal strength may be encoded by the number of spikes in each flip flop cycle, that is a spike count intensity code. Using any realistic neural integrate-and-fire model, as done in [1-2,4-5,42], this neural code can be translated into the corresponding deflections in membrane potential at the single neuron level.

4. Experiment

Behavioral studies may be used to elucidate the algorithm implemented by the loop. In these studies the measurable variables are the trial time and the actions made, and the tunable parameters are the available rewards and efforts associated with the task. Pharmacological agents can be locally applied to validate the putative anatomical locations of the loop's components. Finally, the temporal profiles of S(t), R(t), N(t), $K_{na}(t)$, the value of K_{np} and the sensory coding used can be assessed in electrophysiological studies. We hereby suggest a series of such studies, based on an experimental paradigm refined by Uri Nili at Yadin Dudai's lab. We analyzed an experimental data set kindly provided by Uri Nili, in order to gain basic insights on the loop performance. We first review the results of this analysis, which is provided in detail as supplementary material, then describe the necessary follow-up studies.

In this study, a single male rat is placed in a rectangular maze. A chamber with a food dispenser and a photodetector is situated at both ends of the maze. Whenever the rat reaches one chamber, a few pellets of food are dispensed in the second chamber, at the other end of the maze. Once the rat leaves the chamber, there's a 50% probability for a grid in the middle of the maze to be electrified. When the grid is electrified, a nearby speaker plays a high-pitched tone. The tone only ceases once the rat finishes the trial by reaching the other end of the maze, after passing the electrified grid.

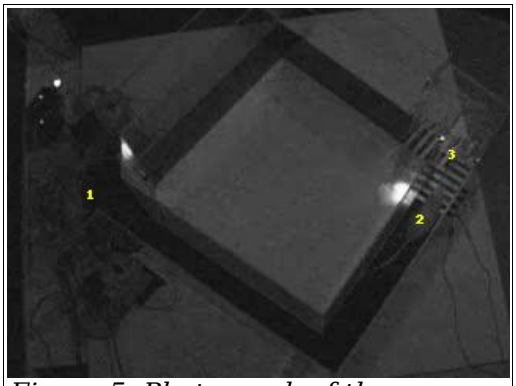

Figure 5: Photograph of the maze
1. chambers with food dispensers
2. hesitating rat
3. Electrified grid

Prior to the experiments, the rat is trained in the same maze, to condition him to link the tone with the electrification of the grid. For low levels of starvation or high electric voltages, the rat may give up crossing the electrified grid and spend the rest of the experiment in his chamber. This fearful response to a conditioned stimulus (CS) is termed **passive coping** [18]. The starvation duration and voltage were tuned for manifestations of hesitance when the grid is electrified. The rat learns to terminate the fear-arousing CS by crossing the maze, a behaviour termed **active coping** [18].

A single rat was tested in four separate experiments. In two experiments, amygdalar activity was down-regulated by a localized injection of either muscimol or bupivacaine. In two earlier experiments, the rat received a dummy injection or an actual injection of saline. Figure 6 shows the resulting trial time histograms. Longer trial times and variability were observed during shock trials (fig. 6 left) than during no-shock trials (fig. 6 right). Shorter trial times and variability were observed when the amygdala was down-regulated ('drugged', fig. 6 bottom) than when it was not ('sober', fig. 6 top). This finding supports the association between amygdalar damage and impulsive decisions, which our model relies upon.

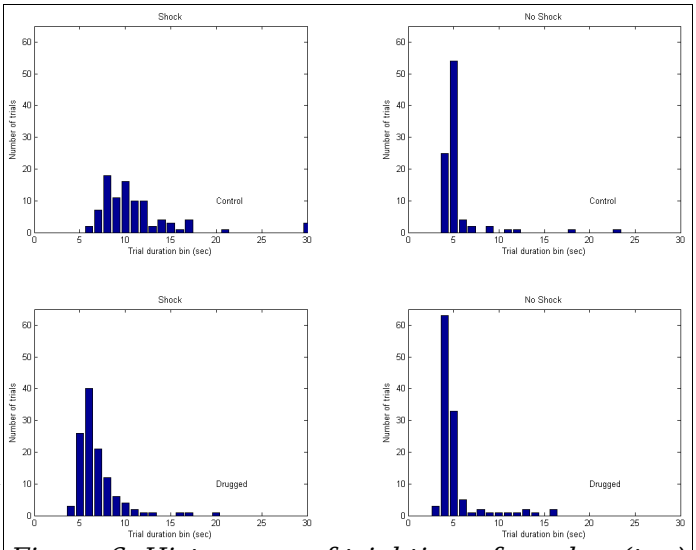

Figure 6: Histograms of trial times for sober (top) and drugged (bottom) experiments. Left – shock trials. Right - no shock trials.

Collating the trial times by the immediate past experience of the rat, we reveal a shorter trial time and a reduced variability when a shock was delivered at the preceding trial (figure 7, blue). This finding suggests that the sober rat is more determined to cross the grid when previously it was shocked. An opposite effect is observed in a variant of the experiment in which the grid is electrified in 50% of the trials at random, with no prior warning (figure 7, red). The randomly shocked rats (n=4) exhibited a longer trial time when shocked at the previous trial, significantly when not shocked at the present trial (the 'no shock after shock' condition). Lacking knowledge about the electrification of the grid until actually reaching it, the rats exhibit a high degree of hesitance and inter-trial variance. The standard error of the mean is almost twice as large in shock trials than in no-shock trials, reflecting a fearful reaction of the rat upon learning of the grid's electrification.

We also analyzed the trial time histograms for two other variants of the experiment: Always shocking the rat (fig. 7, magenta) and never shocking the rat (fig. 7, black). Expectedly, the rats that were never shocked (n=2) exhibited the shortest mean trial times and the least variability. More interestingly, the rats that were always shocked (n=2) exhibited a shorter mean trial time and less variability than those that were only shocked on half of the trials. This finding, along with those regarding the randomly shocked rats, conform with the conclusion that unpredictable stimuli are considered by the amygdala to be more fearful [20].

Finally, we may bound the deliberation time of a sober rat by measuring the difference in its mean trial time across different stimulus conditions. We witness an increase of 6.2 seconds in the mean trial time in "shock after no-shock" trials, with respect to the "no-shock after shock" trials (figure 7, blue). Since we only measure total trial times, we cannot tell how long does the rat spend in sheer hesitation and how long in decisive refusal to cross the maze. Thus only an upper bound can be set on the deliberation time.

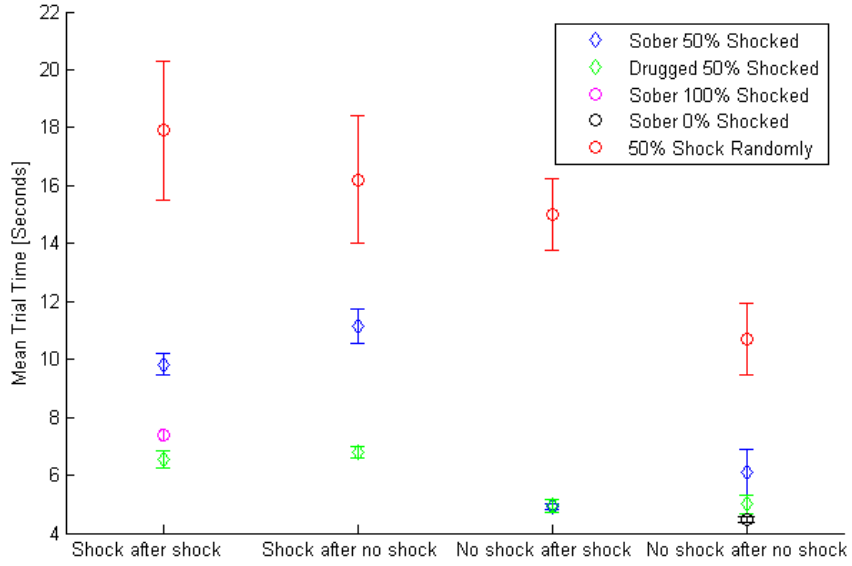

Figure 7: Mean trial time observed in the experiment (blue, green) and its variants (magenta, black, red). Error bars mark standard error of the mean. The sober rat (blue) exhibits a shorter trial time, and a reduced variability, after being shocked at the preceding trial. This behavior is not observed in the rats that are randomly shocked (red). The rats that are always shocked (magenta) exhibit shorter trial time than the randomly shocked rats (red) and the sober rat (blue).

If we attribute the 6.2 seconds increase entirely to a longer deliberation time, it suggests that our hypothetical flip flop spends a considerable time in undetermined state. If its inputs are refreshed at theta range frequencies (~6 Hz), this amounts to about 37 cycles of flip flop operation in metastability, before it is rescued by noise. Circuit operation at higher frequencies, such as the ~40 Hz gamma rhythm, would imply hundreds of flip flop cycles in metastability. This finding argues against a fast amplification of noise level at times of hesitation, at least if our upper bound is reasonably tight.

If noise level is increased at a steady pace, and if its maximal r.m.s. amplitude is assumed to be loosely bound by 50 mV[1], we arrive at an upper bound of about 8 mV/sec for its amplification rate. As single EPSPs in rats are typically slightly larger than 0.8 mV [40], a noise amplification rate of about 0.8 mV per flip flop cycle should enable the circuit to discern a difference of a single EPSP between the competing subthreshold signals. For theta range frequencies of flip flop operation, we arrive at the following estimate for the mean noise amplification rate:

$$(6) \quad \left\langle \frac{d}{dt}\sqrt{\langle N(t)\rangle^2} \right\rangle = v_n \cdot \langle K_{na}(t)\rangle \approx 0.8\text{mV} \cdot 6\,Hz \approx 5\,mV/sec$$

Raising the noise level too fast may lead to a higher rate of incorrect decisions, i.e. decisions made in favor of the weaker subthreshold signal of the two. Suggestively, noise level is amplified rather slowly (i.e. small $K_{na}(t)$) to reduce the resulting error rate.

We found that a pharmacological down-regulation of the amygdala has reduced the mean trial time in the analyzed experiment. In accordance with our proposed model, we predict that a marked increase in trial time will be found following a pharmacological down-regulation of the OFC in rats undergoing a similar experimental paradigm. Once this prediction is validated, extracellular recordings in the OFC and ACC could be used to look for neurons exhibiting graded activity at times of hesitation, using the procedures previously described in [37,41].

If and when we identify neurons with such responsivity, and estimate the temporal profile of $K_{na}(t)$, it should be of great interest to see whether artificial injection of noise leads to faster decision making. For this purpose, electrical microstimulation as practiced for instance in [38] may come of use. By determining the noise amplitude required for optimal decision making, and the corresponding amplitudes of the signals with which it interacts, we could estimate the value of the proportional gain coefficient K_{np}. Alternatively, these electrophysiological recordings may lead to the replacement of $K_{na}(t)$ and K_{np} by an improved model of a noise-level control circuit.

We have suggested that signal strength is encoded by a spike count code, over a time window that corresponds to the duration of each flip flop cycle. The methodology described by Luna et al. [39] could be harnessed to reveal the neural code that matches the behaviour of the rat along each trial. As denoted in [39], a neural code that is based on interactions between multiple neurons, such as a population code or a synchrony code, cannot be decoded by single unit recordings. Thus such an experiment could not determine the uniqueness of a neural code based on the spiking profile of single neurons, but only its feasibility.

In natural environments, increased collection of sensory information may prove useful at times of hesitation. Before overcoming an obstacle to reach for food, it may be beneficial for the organism to look for alternative sources of food, or alternative routes to the known food source which bypass the obstacle. Under this assumption, it may be useful for the organism to be assisted by extrinsic (sensory) noisy sources rather than intrinsic (intracellular) noise sources, as the former ones may also contain information relevant for its dilemma. Unfortunately, due to this assumption we cannot solely rely on behavioral evidence for increased sensory collection at times of hesitation as validating our hypothesis of its application for decision-making, via stochastic resonance. Electrophysiological recordings are thus also required to confirm the algorithm implemented by the loop, whereas behavioral studies alone may suffice to refute it.

1 Resting potential typically lies about 20 mV below threshold, and the hyperpolarized membrane potential is bound by the K^+ reversal potential, that is about 50 mV below threshold.

5. Discussion

The neural mechanisms underlying decision making processes have been investigated by numerous groups in various contexts. A bulk of studies have suggested a bistable module composed of two mutually inhibitory populations of neurons, that can reach a decision and store it [1-5]. While noise has been incorporated into these models, its amplitude has not been previously suggested to be a controlled variable tuned to optimize decision making. We suggest that closed-loop control of sensory noise level enables both enhanced signal detectability and shorter deliberation times.

Moreover, we suggest that the circuit parameters could be tuned, both along evolution and along development, to match the temporal constraints of different decision-making tasks. Specifically, the strength of $K_{na}(t)$ can vary with the importance of fast decision making. Decisions regarding the classification & identification of incoming sensory stimuli are typically taken within tens of milliseconds, up to a few hundreds of milliseconds. Even if we assume that the neural circuitry responsible for sensory decisions operates at gamma frequencies (~40 Hz), its hypothetical flip flop circuit may only spend a few cycles in metastability. Thus $K_{na}(t)$ is expected to be typically larger in sensory decision making, than in motor action decisions that are made over hundreds of milliseconds, up to a few seconds. Consequently, sensory decision-making circuitry is expected to be more prone to errors, and its signal resolution lower. Synaptic plasticity mechanisms may underlie the tuning of the circuit's parameters for different tasks. These predictions may be tested by combined behavioral and electrophysiological studies, similar to those suggested in the previous section.

If and when the proposed model is validated by electrophysiological evidence, psychophysical studies may follow, probing whether a non-zero level of irrelevant data is optimal for decision making. This investigation might lead to the development of cognitive therapeutic tools for patients persistently suffering from detrimental indecisiveness.

To the best of our knowledge, this is the first instance in which stochastic resonance is attributed to decision making processes, though it has been attributed to other high cognitive processes [9-13]. Neural stochastic resonance arises from the collective properties of globally coupled ion channel assemblies [6-7], and does not particularly necessitate the temporal properties of NMDA receptors, upon which earlier models rely [4-5]. While neuronal flip flops have been suggested before [22-24], and stochastic resonance qualified in bistable flip-flop-like systems [14-15], we believe stochastic resonance has not been suggested earlier to play a role in noisy neuronal flip flops. Further experimental and analytic work is required to validate and develop the ideas presented in this work.

Acknowledgments

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